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71 Applicant: FINNIGAN CORPORATION, 335 River Oaks Parkway, San Jose California 95134 (US)

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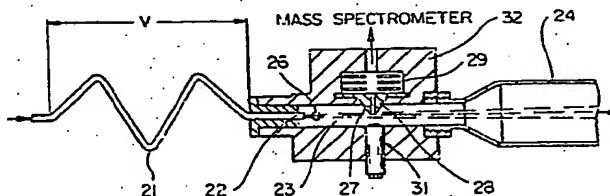
72 Inventor: McFadden, William H., 771 Chopin Drive, Sunnyvale California 94087 (US)
Inventor: Tucker, Michael G., 879 Alcosta Drive, Milpitas California 95035 (US)

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74 Representative: Cross, Rupert Edward Blount et al, BOULT, WADE & TENNANT 27 Farnival Street, London EC4A 1PQ (GB)

64 Thermospray ion sampling device.

57 The performance of a thermospray ion source for liquid chromatograph/mass spectrometers is improved dramatically by providing a voltage gradient across the thermospray jet stream to increase the efficiency of transferring ions of all masses from the thermospray jet stream to the mass spectrometer, and in particular the intensity of high mass ions relative to low mass ions.



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THERMOSPRAY ION SAMPLING DEVICE

The present invention relates to an ion sampling
5 device, and is particularly concerned with improving
the ion yield from a thermospray ion source into a
mass spectrometer during continuous sampling of the
liquid flow from a liquid chromatograph or other
liquid sampling device.

10 Thermospray ion sources for ionizing involatile
molecules from a liquid chromatograph for analysis
in a mass spectrometer have been described in a number
of recent publications; see, for example, Combined
Liquid Chromatograph/Mass Spectrometer for Involatile
15 Biological Samples, C.R. Blakley, J.C. Carmody and
M. L. Vestal, Clinical Chemistry, Vol. 26, No. 10, (1980);
and Characterization of Glucuronides with a Thermospray
Liquid Chromatograph/Mass Spectrometry Interface:
D.J. Liberato, C.C. Fenselau, Marvin. L. Vestal and
20 Alfred L. Yergey, Analytical Chemistry, Vol. 55, No. 11,
September 1983.

Figure 1 shows a typical prior art thermospray liquid chromatograph/mass spectrometer (TSP/LC/MS) ion sampling device interface.

The thermospray source (TSP) includes a vaporizer assembly 10 which includes heaters 11 to rapidly heat a liquid sample flowing through a vaporizer block 12. The heating causes the volatile liquids to vaporize and form a jet stream 13 including vapor and aerosol, which is projected into a chamber 14 at a high velocity and is pumped away via a pumping line 16 leading to a vacuum pump, not shown. At the point of spray formation at the vaporizer tip, gaseous ions are formed from electrolyte ions and from solvated sample ions. These ions are then drawn into an associated mass spectrometer, not shown, by expansion of the vapor through a small orifice 17 in a plate or sampling cone 18 leading to the associated mass spectrometer. With this type of device, only a small fraction, usually less than one percent, of the ions in the vapor are directed into the mass spectrometer. The device can only sample a larger fraction of ions by increasing the diameter or size of the sampling orifice 17 thus imposing abnormally high vacuum pump requirements on the mass spectrometer system communicating with the high pressure region through the orifice. In addition, the device is less efficient for sampling of high mass ions than for low

mass ions which is contrary to accepted good mass spectrometry practice.

According to this invention there is provided a thermospray ion sampling device comprising

5 means to direct a high velocity jet stream into a chamber in a chamber block having an orifice therein through which sample ions from the jet stream leave the chamber, characterised by means to provide a voltage gradient across the jet stream adjacent the

10 orifice thereby to direct sample ions from the jet stream to the orifice.

With the device of this invention the number of ions entering the sampling orifice is greatly increased, and in addition when used with a mass spectrometer the

15 number of high mass ions is increased relative to low mass ions thus greatly improving the quality of the resulting mass spectrum.

The device can receive a liquid sample from any liquid sampling system, such as a liquid chromatograph

20 or the effluent from thin layer chromatographic plate, or from any other chromatographic process or from any automatic or manual sampling device that injects a sample in a liquid stream and forms ions for chemical analysis.

25 The device has high ion extraction efficiency

for all ions and especially for high mass ions from a thermospray ion source that utilizes an electron bombardment process to form ions, in addition to, or exclusive of, the ions formed from electrolyte ions during the thermospray evaporation process. The ions may be formed by electron beam interaction when the solvent is a non-polar normal phase solvent which contains no electrolyte ions and hence only ions from the electron beam interaction and subsequent chemical ion-molecule reactions are present. Said ions may also be formed by electron beam interaction when the solvent is a polar reverse phase solvent containing electrolyte ions and hence the ion plasma is a combination of ions formed by the thermospray process and ions formed by the electron beam interaction and subsequent chemical ion-molecule reactions.

The means to provide a voltage gradient can comprise a repeller electrode mounted in the chamber opposite the orifice, by means of which a voltage gradient is formed that directs ions toward the orifice but does not affect the jet stream of neutral particles. Said repeller electrode may be a flat surface, a concave or convex surface, a sharp point or series of points, or any means that provides a voltage gradient across the jet stream at the sampling orifice.

The invention will now be described by way of example with reference to the drawings, in which:-

Figure 1 is a diagrammatic view of a known thermospray ion source serving as a liquid chromatograph/mass spectrometer interface;

Figure 2 is a diagrammatic view of a thermospray ion source serving as a liquid chromatograph/mass spectrometer interface, embodying the present invention;

Figure 3 shows a repeller electrode for use in the device of Figure 2;

Figure 4 shows an electrically isolated orifice for use in the device of Figure 2; and

Figures 5 and 6 show mass spectrums of a polypropylene polymer mixture obtained without and with use of a device according to the present invention, respectively.

Referring now to Figure 2, a thermospray liquid chromatograph interface is illustrated for use as the ion source for a mass spectrometer. The mass spectrometer can be of any known type. Liquid flow from the chromatograph or liquid sampling device is directed to a vaporizer 21 in the form of a hypodermic tube which may be heated directly by application of a voltage to the ends of the tube. The tube can also be indirectly heated by the transfer of heat from a hot

copper block such as in the prior art vaporizer assembly 10 shown in Figure 1.

The liquid from the liquid sampling device is usually a polar liquid containing an electrolyte
5 although in a few applications the liquid may be a non-polar liquid without an electrolyte. Heat is carefully applied to the vaporizer 21 so as to cause the liquid in the tube to just reach the vaporization point as it emerges from the tip 22 of the tube. The liquid thus
10 emerges in the form of a spray of very fine droplets which rapidly evaporate in a vacuum chamber 23 and are propelled toward a pumping line 24. If the solution is a polar liquid containing an electrolyte, ions are formed in the process of droplet evaporation from the ions in
15 the solution or from the solvated ions in the solution. If the solution is a non-polar liquid, ions are formed by use of an electron beam impinging on the jet stream through an opening 26 in the chamber 23 located slightly past the tip 22.

The ions thus formed are sampled into the mass
20 spectrometer by virtue of expansion of the jet stream as it passes an orifice 27 in a sampling cone 28 which is at a lower pressure. This orifice is the only entrance from the thermospray ion source into electrodes 29 of the mass spectrometer vacuum system and must be kept
25 small so that the large quantity of vapor in the jet

stream does not enter the mass spectrometer proper thus destroying the vacuum necessary for mass spectral operation. In a conventional commercial mass spectrometer the ion sampling efficiency will be low and usually less than one percent of the total ions.

Further, the prior art device described above with reference to Figure 1 in which lateral expansion of the jet stream is the only mechanism for sampling ions, imposes a mass discrimination against high mass ions due to the fact that low mass particles expand more rapidly in the lateral direction while the high mass particles continue forward by virtue of their greater momentum. The sample orifice thus acts as a jet separator but provides an effect contrary to the desired result and thus decreases the concentration of high mass ions.

With the device of this invention the limitations of the prior art device are overcome by use of a repeller electrode 31 set in the chamber block 32 opposite the sampling orifice 27. The repeller electrode 31 may comprise a disc 33, Figure 3, attached to the end of a post 34 mounted in an insulating sleeve 36. The shape and size of the electrode can be selected to optimize the operation for a particular thermospray ion source.

Application of a voltage to the electrode with

respect to the sampling cone 28 (positive voltage for positive ions and negative voltage for negative ions) directs ions toward the sampling cone 28 and provides a much higher sampling efficiency for all ions. In addition, the increased sample ion density is more pronounced for high mass ions.

The sampling cone 28 can be isolated from the chamber block 32 and the repelling voltage applied between the chamber block 32 and the cone 28. Figure 4 shows the cone 28 isolated from the chamber block 32 by insulating material 37 whereby the voltage can be applied directly between the cone 28 and the chamber block 32 rather than between electrode 31 and chamber block 32. Thus, a voltage gradient is established opposite the orifice 27 which connects to the mass analyzer to direct ions through the orifice 27 into the analyzer.

It is further recognized that the efficiency of ion extraction may be increased by programming an increase in the repelling or attracting voltage as the mass spectrometer is scanned to higher masses thus providing an optimum efficiency over a wide mass range.

Referring now to Figures 5 and 6, the mass spectrum of a polypropylene glycol polymer mixture is shown with 0 volts on the repeller electrode 31, Figure 5, and with 150 volts positive on the repeller electrode 31, Figure 6. With 0 volts on the repeller electrode, the most abundant

ion peak is mass 250 with an intensity of 102 counts.
No significant mass peaks are observed above mass 424.
With 150 volts positive on the repeller electrode,
the most abundant ion peak is mass 424 with an intensity
of 2356 counts. Further, it is seen that signal
enhancement increases with mass. For mass 250, the
enhancement is a factor of 16. For mass 424, the
enhancement is a factor of 230. For mass 656, the
enhancement is a factor of 750.

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CLAIMS:

1. A thermospray ion sampling device comprising means (21, 22) to direct a high velocity jet stream into a chamber (23) in a chamber block (32) having an orifice (27) therein through which sample ions from the jet stream leave the chamber (23), characterised by means (31, 28 or 32, 28) to provide a voltage gradient across the jet stream adjacent the orifice (27) thereby to direct sample ions from the jet stream to the orifice (27).
2. A device as claimed in Claim 1, characterised in that said means to provide a voltage gradient comprises a repeller electrode (31) mounted in the chamber block (32) opposite the orifice (27) and electrically isolated from the chamber block (32), the voltage gradient being established between the repeller electrode (31) and the chamber block (32).
3. A device as claimed in Claim 1, characterised in that said means to provide a voltage gradient comprises a conductive cone member (28) providing the orifice (27) and mounted on the chamber block (32) electrically isolated therefrom, the voltage gradient being established between the cone member (28) and the

chamber block (32).

4. In a thermospray ion source of the kind which forms a jet stream, including sample ions, which expands to cause ions to flow through an orifice disposed adjacent to said stream to analyzing means, the improvement comprising means forming a voltage gradient across said stream toward said orifice to impel ions to said orifice.

10

5. A thermospray ion source as in Claim 4, in which said means includes a repeller electrode disposed opposite said orifice, whereby voltage may be applied to the repeller to form the voltage gradient.

15

6. A thermospray ion source as in Claim 1, in which said orifice is formed in a conductive member insulated from the source whereby voltage may be applied to the cone to form the voltage gradient.

20

7. A thermospray ion source as in Claim 1, including means for independently ionizing said jet stream prior to passing said orifice.

25

8. The method of improving the efficiency of a

thermospray ion source of the type which projects a
jet stream past a sampling orifice, which comprises
the step of generating a voltage gradient across
said stream adjacent said orifice to impel ions into
5 said orifice.

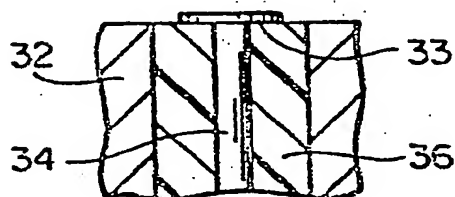
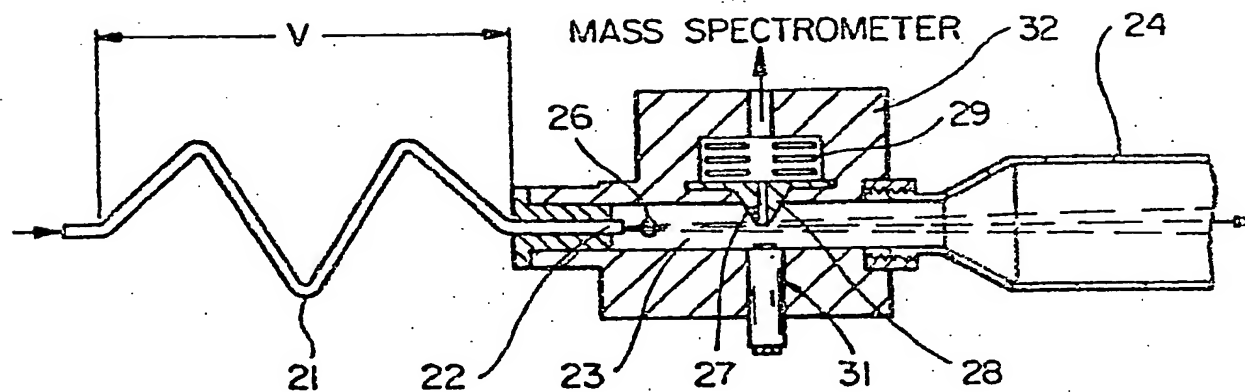
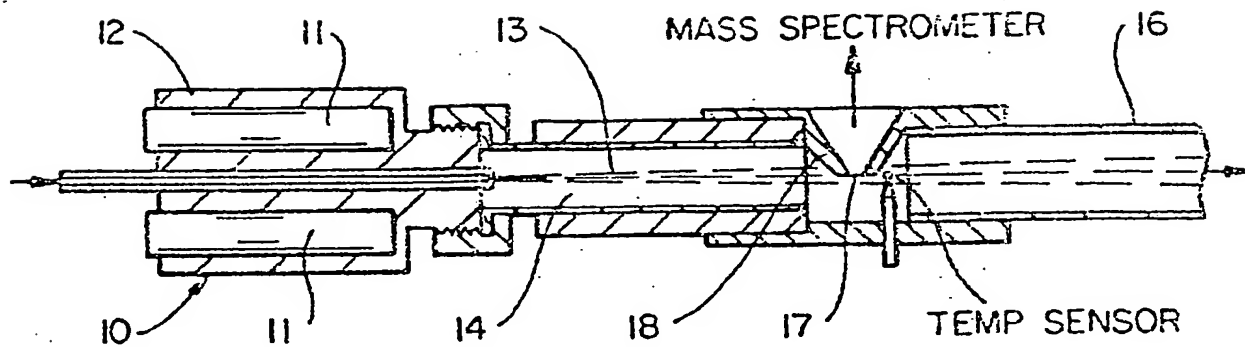
9. The method as in Claim 5, where the voltage
gradient is increased as the analyzing apparatus
analyzes ions of higher masses.

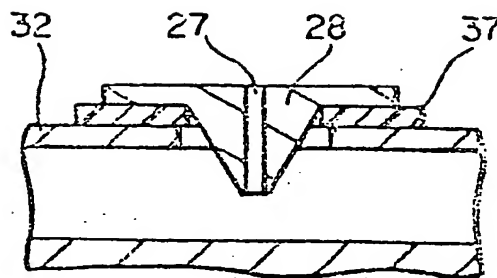
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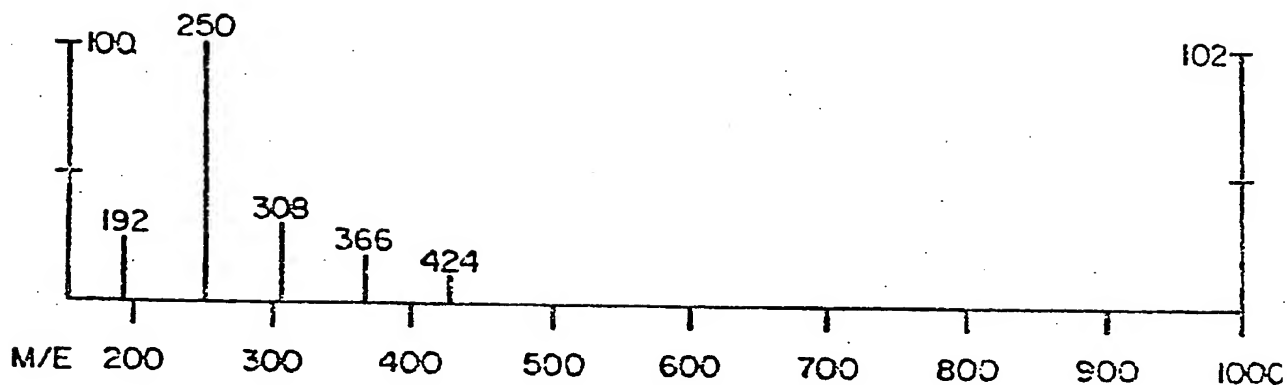
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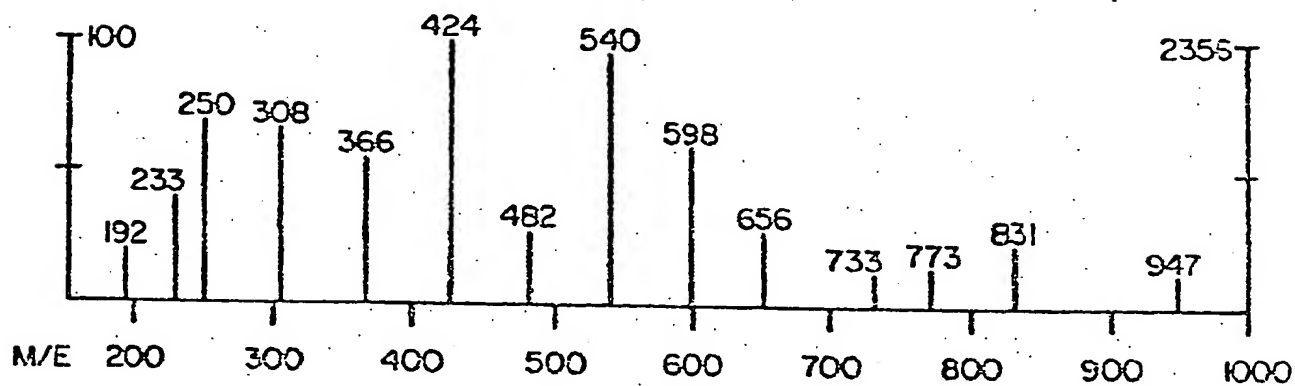




FIG_4



FIG_5



FIG_6



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(71) Applicant: FINNIGAN CORPORATION
355 River Oaks Parkway
San Jose California 95134(US)

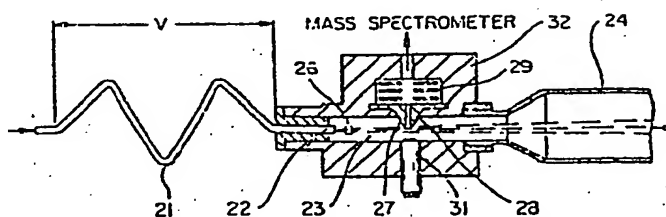
(72) Inventor: McFadden, William H.
771 Chopin Drive
Sunnyvale California 94087(US)

(72) Inventor: Tucker, Michael G.
879 Alcosta Drive
Milpitas California 95035(US)

(74) Representative: Cross, Rupert Edward Blount et al,
BOULT, WADE & TENNANT 27 Farnival Street
London EC4A 1PQ(GB)

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FIG_2

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EUROPEAN SEARCH REPORT

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Application number

EP 85 30 0876

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 4)
Y	US-A-4 160 161 (R.L. HORTON) * column 1, lines 47-54; figure 1 *	1,4	H 01 J 49/04
Y,D	--- ANALYTICAL CHEMISTRY, vol. 55, no. 11, September 1983, pages 1741-1744, American Chemical Society, Washington, DC., US; D.J. LIBERATO et al.: "Characterization of glucuronides with a thermospray liquid chromatography/mass spectrometry interface" * Page 1742, "Experimental sec- tion" * -----	1,4	
			TECHNICAL FIELDS SEARCHED (Int. Cl. 4)
			H 01 J G 01 N
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 26-06-1987	Examiner WINKELMAN, A.M.E.
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X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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